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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,092	10/14/2003	Karen W. Shannon	10030468-1	6820

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EXAMINER	
WHALEY, PABLO S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,092	SHANNON, KAREN W.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/14/03; 4/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

APPLICANT'S ELECTION

Applicant's election with traverse of Group I (Claims 1-16) in the reply filed on 05/31/2006 is acknowledged. The traversal is on the ground(s) that Groups II-V include elements found in Group I, which would facilitate searching. This is not found persuasive because the inventions of Groups I-V are directed to different modes of operation and different effects, as set forth in the restriction requirement mailed 05/08/2006. Furthermore, the examination process requires a search of non-patent literature, U.S. patent publications, U.S. patents, as well as foreign patent literature. The requirement is still deemed proper and is therefore made FINAL.

Claims 17-25 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/31/2006.

CLAIMS UNDER EXAMINATION

An action on the merits of Claims 1-16 follows.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statements filed 4/27/05 and 10/14/03 have been considered in full.

DRAWINGS

Drawings filed 10/14/2003 have been accepted.

OBJECTIONS

Claim 12 is objected to because of the following informalities: Claim 12 is grammatically incorrect, and should recite "plurality." Appropriate correction is required.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 7-16 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 1-4 and 7-14 are directed to a method for identifying a sequence of nucleic acid that is suitable for use as a substrate surface immobilized normalization probe, which does not recite either a physical transformation of matter nor a practical application [i.e. concrete, tangible, and useful result]. Instant claim 1 recites steps comprising identifying probe sequences, empirically evaluating probe sequences, clustering probe sequences, and evaluating non-clustering probes. The claimed method steps do not result in a physical transformation of matter. It is noted that instant claims 1-4 and 7-14 do not require a solid support surface. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a concrete, tangible, and useful result (i.e. a practical application). However, no actual, concrete result is recited in the claims, nor is any useful result "produced" in a tangible form useful to one skilled in the art. For these reasons, the claims are not statutory.

Claim 15 is directed to a computer-readable medium comprising a program. A computer program (i.e. software in the absence of any element to render the software functional) is not statutory. Furthermore, the computer readable medium is not defined by the specification to be a physical object, therefore the claims are not necessarily directed to a physical product, and are nonstatutory for this reason.

Claim 16 is directed to a system comprising a computer-readable medium. The system is not limited to comprise any hardware element or combination of software and hardware such that it is interpreted to be a physical article of manufacture. As the "system" encompasses only software, the claims are not statutory. For the reasons set forth above, the claims are not statutory. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter at 1300 OG 142, Annex IV, Nov. 22, 2005.

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below which leads to the determination that the above claim lacks enablement due to undue experimentation being required to make and use the invention.

Claim 1 is directed to a method of identifying a sequence of a nucleic acid that is suitable for use as a substrate surface immobilized normalization probe. Claim 1 recites steps of (i)

identifying a plurality of candidate probe sequences based on selection criteria, (ii) empirically evaluating probe sequences under different experimental sets, (iii) clustering probe sequences based on empirical data values, and (iv) and evaluating any remaining non-clustering probes for candidate probe sequences. In the instant case, the claimed subject matter lacks enablement for the following reasons:

Regarding step (ii), instant claim 1 requires a plurality of different experimental sets to obtain a collection of empirical data values for each of said candidate nucleic acid probe sequences for each of said plurality of different experimental sets. However, the specification fails to define the metes and bounds of what constitutes such "experimental sets" and how one of ordinary skill in the art would identify or obtain the appropriate "experimental sets" given the lack of description regarding the said experimental sets. What type of experimental sets are required and are the said experimental steps equivalent to experimental conditions, as recited in instant claim 5? Given the nature of the invention, identifying a sequence of a nucleic acid that is suitable for use as a substrate surface immobilized normalization probe based on steps (i)-(iv) generally requires the evaluation of gene expression data. However such limitations are not reflected in the instant claims [Wands factors (2), (3)].

Regarding steps (iii), instant claim 1 requires clustering candidate probe sequences into one or more groups of candidate probe sequences based on empirical values. While the specification does provide a working example [p.32], this example is directed to gene expression experimental data, and thus does not provide sufficient guidance as to how to cluster candidate probe sequence in groups where one or more groups exhibits substantially the same performance across experimental sets based on empirical values. Again, the specification fails to define the metes and bounds of what constitutes such "experimental sets" and "empirical values," and how one of ordinary skill in the art would identify or obtain the appropriate

"experimental sets" and "empirical values" given the lack of description regarding the terms. [Wands factors (2), (4), (8)].

Regarding step (iv), instant claim 1 results in evaluating any remaining non-clustering probes for candidate probe sequences that satisfy a signal intensity threshold and exhibit no signal variation. Firstly, it is unclear how sequences can satisfy a signal intensity threshold, as no correlation has been set forth in the instant claims relating sequences to signal intensity data. Secondly, as no steps directed to obtaining or identifying probes that are "non-clustering" are recited in the instant claims, it is unclear how the evaluation of "any" remaining non-clustering probes "for candidate sequences" results in the identification of candidate probes sequences that are suitable for use as a substrate surface immobilized normalization probe. Thirdly, it is unclear how the "non-clustering probes" are being evaluated. The specification fails to define the metes and bounds of what constitutes "evaluating" such that one of ordinary skill in the art would known how to identify probe sequences that are suitable for use as a normalization probe.

Methods of clustering analysis applied to gene expression data are well-known in the art [Ben-dor et al., Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297] and [Alon et al., Cell Biology, 1999, Vol. 96, p.6745-6750]. Such methods disclose steps directed to (i) determination of gene expression data by measuring expression levels experimentally (ii) calculation of similarity matrices comprising expression patterns, (iii) clustering gene based on similarity data or expression data (i.e. intensity data) using clustering algorithms, and (iv) representing constructed solutions visually as histograms or distributions. Furthermore, most clustering analysis experiments consist of some comparative steps (e.g. mutants compared to a reference) and evaluation of data using some statistical correlation methods as well. Kane et al. [Nucleic Acids Research, 2000, Vol. 28, p.4552-4557], for example, teach methods of

oligonucleotide probe design and assessment, including steps comparison of probe sensitivities [Fig. 1]. Thus, specification does not provide sufficient guidance as to how to identify a sequence of a nucleic acid that is suitable for use as a substrate surface immobilized normalization probe based on clustering of candidate probe sequences [Wands factors (1), (2), (6), (7)].

Despite the high level of skill in the art, as the specification does not disclose sufficient guidance as to how one of skill in the art can identify a sequence of a nucleic acid that is suitable for use as a substrate surface immobilized normalization probe, and as the instant claims do not recite steps consonant with the identification of a sequence of a nucleic acid, as set forth above, it would require undue experimentation by one of skill in the art to predictably practice the instantly claimed invention. [Wands factors (1), (2), (6), (7)].

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a method for identifying a sequence of a nucleic acid" in the preamble. As the method steps result in "evaluating any remaining non-clustering probes..." and do not result in the identification of a sequence, it is unclear in what way the steps of claim 1 achieve the purpose of the preamble. Clarification is requested.

Claim 1, step (b), recites the limitation "a plurality of different experimental sets." It is unclear as to the intended meaning of "experimental sets" in this context, as this could be interpreted to mean physical groups, experimental setups, or otherwise. Clarification is requested.

Claim 1, step (b), recites "evaluating probe sequences...to obtain a collection of...data...for...probe sequences for...different experimental sets." It is unclear in what way this limitation further limits the evaluated probe sequences. Furthermore, it is unclear exactly what the collection of data is obtained for. Clarification is requested.

Claim 1, step (d), recites the limitation "evaluating any remaining non-clustering probes." It is unclear whether said non-clustering probes are being evaluated based on signal intensity threshold, signal variation, or some other method. Clarification is requested.

Claim 1, step (d), recites the limitation "evaluating any remaining non-clustering probes." As there is no previous recitation of non-clustering probes or any step directed to obtaining "non-clustering probes", there is lack of antecedent basis for this limitation. Furthermore, it is unclear in what way this limitation further limits the said candidate probes. Clarification is requested.

Claim 1, step (d), recites the limitation "said plurality that are suitable for use...as a probe." It is unclear whether the said "plurality" is referring to non-clustering probes, candidate probes, clustered probes, or otherwise. Clarification is requested.

Claim 3 recites the limitation "wherein...selection criteria...are employed is said identifying step (a)." It is unclear whether this is an additional method step or a further limitation to parent claim 2. It is noted that there appears to be a grammatical error in claim 3 as well. Clarification is requested.

Claim 5 recites the limitation "said...experimental conditions." As parent claim 1 recites "experimental sets," there is lack of antecedent basis for this limitation. Furthermore, it is unclear in what way this limitation further limits the said candidate probes. Clarification is requested.

Claim 6 recites the limitation "each member...is a different tissue/cell line differential gene expression assay." It is unclear whether each member is a different tissue, a different cell line, a differential gene expression assay, or a combination of these. Clarification is requested.

Claim 7 recites "obtaining an expression vector...using...empirical data values", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Clarification is requested.

Claim 10 recites the limitation "sequence is considered to exhibit." It is unclear whether this is a limitation of the intended method or an actual physical step. Furthermore, it is unclear as to the applicant's intended meaning of a sequence being "considered to exhibit." Clarification is requested.

CONCLUSION

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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8/7/06